



UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office

Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/913,257	12/05/97	BIERSKCKY	K 697.002US1

HM32/1230
SCHWEGMAN LUNDBERG WOESSNER & KLUTH
PO BOX 2938
MINNEAPOLIS MN 55402

EXAMINER

DEEMIE, R

ART UNIT PAPER NUMBER

1621

DATE MAILED:

12/30/98

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
08/913,257

Applicant(s)
Giersckey et al.

Examiner
Robert Deemie

Group Art Unit
1621



☒ Responsive to communication(s) filed on Dec 5, 1997

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-20 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-20 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Art Unit: 1621

DETAILED ACTION

Priority

1. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 08/913,257, filed on December 5, 1997.

Specification

2. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.
3. Applicant is reminded of the proper content of an Abstract of the Disclosure.

In chemical patent abstracts for compounds or compositions, the general nature of the compound or composition should be given as well as its use, *e.g.*, "The compounds are of the class of alkyl benzene sulfonyl ureas, useful as oral anti-diabetics." Exemplification of a species could be illustrative of members of the class. For processes, the type reaction, reagents and process conditions should be stated, generally illustrated by a single example unless variations are necessary.

Information Disclosure Statement

4. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be

Art Unit: 1621

incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 112

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 2 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds of formula I, does not reasonably provide enablement for the R1 group "optionally interrupted by oxygen, nitrogen, sulfur or phosphorous atoms." The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with this claim.

Art Unit: 1621

One oxygen atom interrupting an alkyl chain is a dialkyl ether, which as a class are generally unreactive and thermally stable. Two oxygen atoms interrupting an alkyl chain form a dialkyl peroxide. The decreased thermodynamic stability of peroxides is such that "All organic peroxides should be regarded as being potentially explosive." Three or more oxygen atoms interrupting an alkyl chain are more unstable than dialkyl peroxides. (Davies, A. G.; *Organic Peroxides*; Butterworth and Co. London, 1961; p. 196).

Nitrogen and phosphorous atoms are tri-valent elements of Group 15; they do not form saturated dialkyl compounds (Cotton, F. A. et al. *Advanced Inorganic Chemistry*, 5th ed. Wiley, New York; 1988; pp. 305-309, 382-386).

There is no guidance in the specifications on the number of adjacent oxygen, nitrogen, sulfur or phosphorous atoms that are used as interrupting atoms, nor are any details disclosing the synthesis of compound of the genus Formula I that use oxygen, nitrogen, or phosphorous atoms as alkyl interrupting atoms. Without this guidance, no one skilled in the art can add more than two oxygen atoms, or any nitrogen or phosphorous atom as an interrupting atom in an alkyl chain.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In formula I of claim 2, the broad group R1 "may represent alkyl groups optionally

Art Unit: 1621

substituted by hydroxy." The language "may represent" is vague and indefinite, since any person skilled in the art would not know what other possible functional groups R1 represents. The examiner suggests deleting "may" from the definition of R1, as the phrase "R1 represent alkyl groups optionally substituted with [various functional groups]" is not indefinite.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-8 and 19-20 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Salerni (Salerni, O. L. et al. *J. Chem Soc. (C)*; 1968; p. 1399). Salerni shows the synthesis of methyl 5-(benzyl-methyl amino)-4-oxo pentanoate (p.1400).

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Art Unit: 1621

13. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35

U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

14. Claims 10-15, and 17-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kennedy (Kennedy et al. U.S. 5,079,262) as applied to claims 10-13, 15, 17, and 18 above, and further in view of Ariens, E. J. (*Drug Design*; Ariens, E. J. Ed.; Academic Press; New York, 1971). Kennedy shows a method of detecting and treating tissue abnormalities by topical administration of 5-aminolevulinic acid, followed by exposure of the treated area to photoactivating light (col 6:40-45) in the range of 350-640 nm. Ariens broadly teaches how to modify part of a pharmaceutically active molecule that hinders tissue absorption by masking the offending functional group. Ariens discusses changing COOH-groups to esters; drug transport of an inactive "transport form" of a drug into an intercellular compartment, and bioactivation of the drug by cleaving the masking moiety (p. 8-11, 70-71).

In the instant case, the alkyl groups (R1) in Formula I mask the lipophobic carboxylic acid functional group by formation of an ester. This reduces the molecule's polar nature, allowing better penetration of cell membranes. The alkyl group are then cleaved at physiological pH's to form the pharmaceutically active 5-aminolevulinic acid. The method used to treat tissue

Art Unit: 1621

abnormalities was set forth by Kennedy. It would have been obvious to one skilled in the art to modify 5-aminolevulinic acid by esterifying the acid in order to increase 5-aminolevulinic acid concentration levels in the target cells.

15. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Morrison, (Morrison, R.T. et al.; *Organic Chemistry 3rd Ed.*; Allyn and Bacon; Boston; 1973). Morrison teaches the formation of esters from acyl halides and anhydrides (pp. 666, 668-9, 673), and also the formation of addition salts of amines (p 631).

16. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kennedy, and further in view of Ariens, and further in view of Sandborn (Sandborn E. U.S. 4,575,515). The treatment of disorders or abnormalities requires penetration of a composition into the target tissues (vide supra paragraph 14). Sandborn shows the use of DMSO as a surface-penetrating agent in the delivery of medicaments through the skin (col 3:5-63). It would have been obvious to one skilled in the art to increase the skin tissue penetration of the composition in Kennedy as modified by Ariens by using DMSO as a surface-penetration assisting agent.

17. The prior art made of record and not relied on is considered pertinent to applicant's disclosure. Gawell (Gawell, L. et al. *Acta Chemica Scandinavica*; 43; 1989; p. 476) show the synthesis of 2-(2-pyridyl)ethyl 5-(N-benzyloxocarbonyl)-amino-4-oxo-pentanoate and ethyl 5-(3-bromo-2,6-dimethoxybenzamido)-4-oxo-pentanoate. Schulz (Schulz, G. et al. *Chem. Ber.*; 113 (2); 1980; p. 770) show the synthesis of the hydrogen bromide salt of ethyl 5-amido-4-oxo-pentanoate and ethyl 5-((1,1,1-triphenylmethyl)amido)-4-oxo-pentanoate.

Art Unit: 1621

Conclusion

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Deemie whose telephone number is (703) 305-5734. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Geist, can be reached on (703) 308-1701. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.



GARY GEIST
SUPERVISORY PATENT EXAMINER
TECH CENTER 1600